

**REMARKS**

Claims 22-50 are pending. By this Amendment, claims 22-24, 30-32, 36, 40 and 43-47 are amended and claims 48-50 are added. No new matter is added.

**I. Specification Objection**

The specification is objected to because the Abstract is missing and because the title is allegedly not aptly descriptive. By this Amendment, an Abstract is added. Although Applicants do not agree with the title objection, the title is amended in order to expedite prosecution. Reconsideration and withdrawal of the objection are respectfully requested.

**II. "H" Is Not a Substituent**

By this Amendment, the specification is amended to explicitly state that the term "substituent" does not include hydrogen. This amendment does not introduce new matter, as it merely makes explicit that which was at least implicit, for the reasons discussed below.

The specification clearly describes a compound containing a cyclic ring that is substituted with 1 to 3 groups that limit the diffusion of the  $\alpha$ -keto acid produced by the deamination of the compound. The examples describe substituted tyrosine, tryptophan and histidine, each of which contains four or more hydrogen groups. Thus, it is clear that the inventors were not considering hydrogen to be a substituent that limits diffusion. In addition, attached hereto is an excerpt from A Dictionary of Chemistry defining the term substituent as "[a]n atom or group regarded as having replaced a hydrogen atom in a chemical derivative." Thus, amending the specification to clearly recite that hydrogen is not a substituent does not introduce new matter into the specification.

III. §112, First Paragraph, Rejections

Claims 22-47 are rejected under the written description requirement of 35 U.S.C. §112, first paragraph. Applicants respectfully traverse the rejection.

The Office Action indicates that the phrase "...group other than hydrogen that, as compared to where X is hydrogen" lacks written description. Although Applicants do not agree, this feature is removed from the claims to expedite prosecution. By this Amendment, claims 22, 30 and 47 are amended in order to clarify that diffusion is limited as compared to an L-amino acid having a cyclic radical that has not been substituted. Explicit support for this claim feature can be found at page 5, line 33 to page 6, line 7, of the specification.

For at least these reasons, Applicants submit that claims 22-47 satisfy the written description requirement of §112, first paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

IV. §112, Second Paragraph Rejections

Claims 22-47 are rejected under 35 U.S.C. §112, second paragraph as being indefinite. Applicants respectfully traverse the rejection.

The Office Action states that claims 22-47 are indefinite because there is inconsistency in the claims regarding what enzyme is intended. Applicants assert that the particular enzyme or enzyme activity is clear to one skilled in the art. Specifically, each of claims 22, 30 and 47 recite the feature "...that limit the diffusion in the culture medium of the α-keto acid produced by the deamination of the compound." (Emphasis added). One skilled in the art would understand the enzyme to be a deaminase, and the activity to be deaminase activity. However, in an effort to expedite prosecution, the claims are amended to explicitly recite deaminase in the preamble.

The Office Action also states that claims 22-47 are indefinite for reciting the phrase "...group other than hydrogen that, as compared to where X is hydrogen." Although

Applicants do not agree, this feature is removed from the claims to expedite prosecution. By this Amendment, claims 22, 30 and 47 are amended to recite that R in the general formula (I) represents an organic radical containing a cyclic ring, said cyclic ring being substituted with 1 to 3 substituents (claim 22) or 2 or 3 substituents (claim 30) or 1 substituent (claim 47) that are identical or different and each of which limits the diffusion in the culture medium of the  $\alpha$ -keto acid produced by the deamination of the at least one detection agent, as compared to where each of said substituents is not present. Explicit support for this claim feature can be found at page 5, line 33 to page 6, line 7, of the specification.

It is clear to one skilled in the art of detecting enzymatic activity that the claimed substituents are chemical groups added to the cyclic ring that limits diffusion of the deaminated  $\alpha$ -keto acid. One skilled in the art of detecting enzymatic activity would be able to determine what groups may or may not be used with the claimed invention based on the specification and in particular the disclosure of sample chemical groups that limit the diffusion. See page 11, lines 8-12, and page 14, line 38, of the specification and new claims 48-50.

As discussed in previous responses, and as acknowledged in the Office Action, Applicants also describe the claimed substituents functionally, with support in the specification and a description of how to locate substituents appropriate for use in the claimed invention. The claimed substituents would be clear to one skilled in the art based on (1) the disclosure of specific examples of the claimed substituents, (2) the functional description of the claimed substituents, and (3) the description of routine experiments to find the claimed substituents.

The Office Action also generally states that the term "revealing agent" is not a term of art, and that "what is revealed by what is not seen as claimed;" however, the Office Action does not apply this rejection to specific claims. For example, claim 30 does not recite a

revealing agent. However, Applicants respectfully disagree that the term "revealing agent" is unclear.

Regardless of whether the term "revealing agent" is a "term of art," those skilled in the art understand the concept of detecting the presence of an enzyme based on the biological activity of the enzyme. As described in detail at page 1, line 35 to page 2, line 13, of the specification, the biological activities of an enzyme can be demonstrated in various ways. In each of these methods, the action of the target enzyme is detected (when the enzyme is present), and the detection is revealed to the experimenter as a colored or fluorescent product. One skilled in the art would understand that a revealing agent is a color or fluorescent indicator.

Although the Office Action cites page 7 of the specification, in which Applicants identify a cation salt as an example of such a revealing agent, the Office Action fails to acknowledge additional areas of the specification where Applicants discuss revealing agents, such as at pages 1-4. In order to make explicit that which was implicit, Applicants amend claims 22, 40 and 47 to further define the term "revealing agent" as being a color or fluorescent indicator.

For at least the reasons discussed above, claims 22-47 satisfy the requirements of §112, second paragraph. Reconsideration and withdrawal of the rejections are respectfully requested.

V. §102 Rejections

Claims 30, 31 and 45-47 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 4,937,352 to Voelter (Voelter), U.S. Patent No. 4,507,230 to Tam et al. (Tam), U.S. Patent No. 5,668,254 to Deghengi (Deghengi) and U.S. Patent No. 5,173,434 to Morris et al. (Morris). Applicants respectfully traverse the rejections.

A. Claims 30, 31, 45 and 46

Claim 30 is directed to a compound having the general formula (I), in which R represents an organic radical containing a cyclic ring substituted with 2 or 3 substituents, each of which limits the diffusion in the culture medium of the  $\alpha$ -keto acid produced by the deamination of the at least one detection agent, as compared to where each of said substituents is not present. However, each of Voelter, Deghengi and Morris discloses a compound substituted with only one substituent.

The Office Action cites Voelter's disclosure of histidine derivatives as anticipating claim 30; however, each of these compounds only have one substituent. The Office Action cites Deghengi's disclosure of 2-methyltryptophan as anticipating claim 30; however, this compound only has one substituent -- a single methyl group. The Office Action cites Morris' disclosure of p-nitrophenylalanine as anticipating claim 30; however, this compound only has one substituent -- a single nitro group.

The Office Action asserts that the claims encompass hydrogen as a group that can serve as a second substituent in the cited references. For example, regarding Morris, the Office Action seems to indicate that the single nitro group present on the phenylalanine ring in combination with a hydrogen group present on the phenylalanine ring anticipates the claimed invention and specifically the claimed feature "an organic radical containing a cyclic ring substituted with 2 or 3 substituents." However, as discussed above, hydrogen is clearly excluded from the claimed substituents.

In addition, even if hydrogen is impermissibly considered a claimed substituent, the cited references teach away from the claimed invention by disclosing compounds having greater than 2 or 3 substituents. Using Morris' disclosure of p-nitrophenylalanine as an example, the six-member cyclic ring of the phenylalanine includes a nitro group ( $\text{NO}_2$ ) on one member of the ring, and at least one hydrogen on four of the other five members of the ring.

Thus, if hydrogen were impermissibly considered a claimed substituent, Morris would teach a compound having at least five substituents – which is clearly outside of the claimed range.

Similarly, the Office Action cites Tam's disclosure of 3-benzyltyrosine as anticipating claim 30. However, Tam does not teach or suggest a compound in which at least one of the substituents is naphthalene-sulfonyl, tosyl-sulfonyl or mesitylene-sulfonyl.

For at least the reasons discussed above, claim 30 is not anticipated by the cited references. Claims 31, 45 and 46 depend from claim 30 and thus include all of its limitations. Accordingly, these dependent claims are not anticipated by the cited references for at least the same reasons as claim 30. Reconsideration and withdrawal of the rejection are respectfully requested.

B. Claim 47

Claim 47 is directed to a detection agent comprising at least one compound having the general formula (I) in which R represents an organic radical containing a cyclic ring, substituted with 1 substituent, and a revealing agent comprising a color or fluorescent indicator that produces a coloration or fluorescence with the at least one compound. Thus, the claimed detection agent includes both the claimed compound and the claimed revealing agent.

None of Voelter, Tam or Deghengi discloses a detection agent, and none of these three references disclose a detection agent comprising the claimed compound and the claimed revealing agent. Although Morris discloses of p-nitrophenylalanine, Morris does not teach a detecting agent comprising the claimed compound and the claimed revealing agent. In fact, Morris teaches away from the claimed invention by disclosing that a bacterial isolate is added to a medium containing p-nitrophenylalanine, and color is detected after the subsequent addition of NaOH. See column 13, lines 11-15 of Morris. Thus, Morris teaches away from

the claimed invention by requiring that the compound and the revealing agent be separate compositions, added separately from one another.

For at least these reasons, claim 47 is not anticipated by the cited references.

Reconsideration and withdrawal of the rejection are respectfully requested.

VI. §103 Rejections

Claims 22, 23, 25-29 and 36-44 are rejected under 35 U.S.C. §103(a) as being unpatentable over Morris in view of U.S. Patent No. 3,725,203 to Sellers (Sellers).

Applicants respectfully traverse the rejection.

A. Claims 22, 23 and 25-29

Claim 22 is directed to a method for detecting and identifying and/or quantifying an enzymatic activity of a microorganism, comprising preparing a culture medium comprising at least one detection agent that is an L-amino acid of the general formula (I) in which R represents an organic radical containing a cyclic ring, the cyclic ring being substituted with 1 to 3 substituents that are identical or different and each of which limits the diffusion in the culture medium of the  $\alpha$ -keto acid produced by the deamination of the at least one detection agent, as compared to where each of said substituents is not present.

Morris teaches p-nitrophenylalanine. Thus, in Morris, the cyclic ring is substituted with a nitro group. One skilled in the art would understand that culture media are hydrophilic. In addition, one skilled in the art would understand that hydrophilic compounds would diffuse in a hydrophilic media, and hydrophobic molecules would diffuse little or not at all. As discussed in previous Responses, nitro groups are hydrophilic groups that would diffuse in culture medium. See the specification at page 4, lines 3-9 and 27-33. Thus, Morris does not teach or suggest a compound that is substituted with a group that limits diffusion. In fact, Morris teaches away from the claimed invention by disclosing p-nitrophenylalanine.

Sellers does not overcome the deficiencies of Morris. In particular, Sellers discloses unsubstituted amino acids, and therefore does not overcome Morris' teaching of a hydrophilic nitro groups ( $\text{NO}_2$ ) that would diffuse in culture medium.

For at least these reasons, Morris, alone or in combination with Sellers, does not teach or suggest every feature of claim 22. Thus, claim 22 is patentable over Morris, alone or in view of Sellers. Claims 23 and 25-29 depend from claim 22, and thus include all of its features. Accordingly, these dependent claims are patentable over Morris, alone or in view of Sellers, for at least the same reasons as claim 22. Reconsideration and withdrawal of the rejection are respectfully requested.

B. Claims 36-44

For at least the reasons discussed above in Section V A, Morris does not teach or suggest every feature of claim 30. Specifically Morris does not teach or suggest a compound having a cyclic ring substituted with 2 or 3 substituents.

In addition, for at least the reasons discussed above in Section VI A, Morris does not teach or suggest every feature of claim 30. Specifically, Morris does not teach or suggest a cyclic ring substituted with 2 or 3 substituents that each limit the diffusion in the culture medium of the  $\alpha$ -keto acid produced by the deamination of the compound.

Sellers does not overcome the deficiencies of Morris. Sellers disclosure of unsubstituted amino acids does not teach or suggest a cyclic ring substituted with 2 or 3 substituents that limit the diffusion in the culture medium of the  $\alpha$ -keto acid produced by the deamination of the compound.

For at least these reasons, Morris, alone or in view of Sellers, does not teach or suggest every feature of claim 30. Thus, claim 30 is patentable over Morris, alone or in view of Sellers. Claims 36-44 depend from claim 30, and thus include all of its limitations. Accordingly, these dependent claims are patentable over Morris, alone or in view of Sellers,

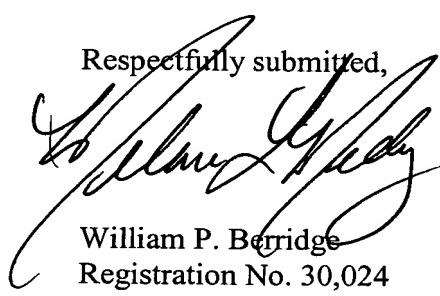
for at least the same reasons as claim 30. Reconsideration and withdrawal of the rejection are respectfully requested.

VII. Conclusion

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number set forth below.

Respectfully submitted,

  
William P. Berridge  
Registration No. 30,024

Melanie L. Mealy  
Registration No. 40,085

WPB:MLM/jam

Attachments:

Abstract  
Chemical Dictionary Excerpt

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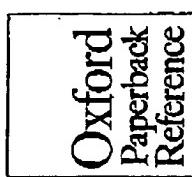
A Dictionary of  
**Chemistry**

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FOURTH EDITION

Edited by  
JOHN DANTITH

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## Preface.

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This dictionary was originally derived from the *Course Science Dictionary*, first published by Oxford University Press in 1984 (fourth edition, reitled *Dictionary of Science*, 1990). It consisted of all the entries relating to chemistry in this dictionary, including physical chemistry, as well as many of the terms used in biochemistry. For this fourth edition we have updated existing entries where necessary and added many new entries. In addition we have included special feature articles on important topics as well as several chronologies tracing the history of some topics. A further innovation in this edition is the introduction of short biographical entries on the scientists and other scientists who have been responsible for the development of the subject.

An asterisk placed before a word used in an entry indicates that this word can be looked up in the dictionary and will provide further explanation or classification. However, not every word that appears in the dictionary has an asterisk placed before it. Some entries simply refer the reader to another entry, indicating either that they are synonyms or abbreviations or that they are most conveniently explained in one of the dictionary's longer articles or features. Synonyms and abbreviations are usually placed within brackets immediately after the headword. Terms that are explained within an entry are highlighted by being printed in italic type.

The more physical aspects of physical chemistry and the physics itself will be found in *A Dictionary of Physics*, which is a companion volume to this dictionary. A *Dictionary of Biology* contains a more thorough coverage of the biological and biochemical entries from the *Dictionary of Science* together with the entries relating to biology.

SI units are used throughout this book and its companion volumes.

J.D.  
2000

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**strontium hydrogen carbonate**

with strontium carbonate, oxide, or hydroxide. Strontium chloride is used for military flares.

**strontium hydrogencarbonate (strontium bicarbonate)** A compound,  $\text{Sr}(\text{HCO}_3)_2$ , which is stable only in solution. It is formed by the action of carbon dioxide on a suspension of strontium carbonate in water. On heating, this process is reversed.

**strontium oxide** (strontia) A white compound,  $\text{SrO}$ ; rd. 47; m.p. 243°C, b.p. 300°C. It can be prepared by the decomposition of heated strontium carbonate, hydroxide, or nitrate, and is used in the manufacture of other strontium salts, in pigments, soap, and greases, and as a drying agent.

**strontium sulphate** A white solid,  $\text{SrSO}_4$ ; rd. 396; m.p. 1600°C. It can be

made by dissolving strontium oxide, hydroxide, or carbonate in sulphuric acid. It is used as a pigment in paints and ceramic glazes and to provide a red colour in fireworks.

**structural formula** See formula.

**structural isomerism** See isomerism.

**structure factor** A quantity denoted  $F_{h\bar{k}\bar{l}}$  where  $h$ ,  $k$ , and  $l$  are the Miller indices of the crystal, which occurs in "X-ray crystallography and other experiments involving scattering in crystals."  $F_{h\bar{k}\bar{l}}$  is defined by the equation:

$$F_{h\bar{k}\bar{l}} = \sum_i f_i \exp[2\pi i(\bar{h}\bar{A}_i + \bar{k}\bar{B}_i + \bar{l}\bar{C}_i)]$$

where the sum is over all atoms of the unit cell and  $f_i$  is the scattering factor for atom  $i$  defined by:

$$f_i = -\frac{4\pi}{\lambda} \int_0^{\infty} (\rho \sin k_i r)^2 dr$$

Here  $k = 4\pi/\lambda$ , where  $\lambda$  is the Bragg angle [see Bragg's law],  $\rho$  is the wavelength of the X-rays, and  $\rho$  is the electron density distribution of the atom  $i$ . The structure factor is used in Patterson synthesis [see Patterson functions].

**strychnine** A colorless poisonous crystalline alkaloid found in certain plants.

**styrene** See phenylethene.

**subadjacent orbitals** The next-highest occupied molecular orbital ( $\text{NHO}_{\text{MO}}$ ) and the second-lowest unoccupied molecular orbital ( $\text{SUHO}$ ). In certain cases these subadjacent orbitals are significant in "frontier-orbital theory."

**subliminate** A solid formed by sublimation.

**submillimetre waves** Electromagnetic radiation with wavelengths below one millimetre (and therefore frequencies greater than 300 gigahertz), extending to radiation of the far infrared. A source of

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**sulphanes**

submillimetre radiation is a medium pressure mercury lamp in quartz. Submillimetre waves can be detected by a "Golay cell."

**subshell** See atom.

**substantive dye** See dyes.

**substantivity** The affinity of a dye for its substrate.

**substituent** 1. An atom or group that replaces another in a substitution reaction. 2. An atom or group regarded as having replaced a hydrogen atom in a chemical derivative. For example, dibromobenzene [ $\text{C}_6\text{H}_4\text{Br}_2$ ] is a derivative of benzene with bromine substituents.

**substitution reaction** (displacement reaction) A reaction in which one atom or molecule is replaced by another atom or molecule. See: electrophilic substitution; nucleophilic substitution.

**substrate** 1. The substance that is affected by the action of a catalyst, for example, the substance upon which an enzyme acts in a biochemical reaction. 2. The substance on which some other substance is adsorbed or on which it is absorbed. Examples include the material to which a dye is attached, the porous solid absorbing a gas, and the "matrix trapping isolated atoms, radicals, etc.

**succinic acid** See butanedioic acid.

**sucrose** (cane sugar; beet sugar; saccharose) A sugar comprising one molecule of glucose linked to a fructose molecule. It occurs widely in plants and is particularly abundant in sugar cane and sugar beet (15–20%), from which it is extracted and refined for table sugar. If heated to 200°C, sucrose becomes caramell.

**sugar (sacharide)** Any of a group of water-soluble carbohydrates of relatively low molecular weight and typically having a sweet taste. The simple sugars are called monosaccharides. More complex sugars comprise between two and ten monosaccharides linked together: disaccharides contain two, triaccharides three, and so on. The name is often used to refer specifically to sucrose (table sugar).

**sugar oil lead** See lead(II) ethanoate.

**sulphite drugs** See sulphonamides.

**sulphamic acid** A colourless crystalline solid  $\text{NH}_2\text{SO}_3\text{OH}$ , which is extremely soluble in water and normally exists as the zwitterion  $\text{H}_3\text{N}^+\text{SO}_3^-$ . It is a strong acid, readily forming sulphamate salts. It is used in electroplating, hard-water scale removers, herbicides, and artificial sweeteners.

**sulphanes** Compounds of hydrogen and sulphur containing chains of sulphur atoms. They have the general formula  $\text{H}_2\text{S}_n$ . The simplest is hydrogen sulphide,  $\text{H}_2\text{S}$ ; other members of the series are  $\text{H}_2\text{S}_2$ ,  $\text{H}_2\text{S}_3$ ,  $\text{H}_2\text{S}_4$ , etc. See sulphides.